```
**********STN Columbus **********

FILE 'MEDLINE'
FILE 'JAPIO'
FILE 'BIOSIS'
FILE 'SCISEARCH'
FILE 'WPIDS'
FILE 'CAPLUS'
FILE 'EMBASE'
=> voltage-gated sodium channel# or voltage gated sodium channel#
L1      3230 VOLTAGE-GATED SODIUM CHANNEL# OR
VOLTAGE GATED SODIUM CHANNEL#

=> l1 and (beta3 or beta 3 or beta-3)
  5 FILES SEARCHED...
L2      65 L1 AND (BETA3 OR BETA 3 OR BETA-3)

=> l2 and (amplification or amplify)
L3      1 L2 AND (AMPLIFICATION OR AMPLIFY)

=> dup rem l2
PROCESSING COMPLETED FOR L2
L4      29 DUP REM L2 (36 DUPLICATES REMOVED)

=> d l3

L3  ANSWER 1 OF 1  WPIDS  COPYRIGHT 2003 THOMSON
DERWENT on STN
AN  2000-665241 [64]  WPIDS
DNC C2000-201571
TI  Novel nucleic acids encoding a  ***beta*** - ***3***  subunit
from a
    ***voltage*** - ***gated***  ***sodium***  ***channel*** ,
and
    their corresponding polypeptides, useful for detecting and treating
sodium
    channel-associated conditions, e.g. pain, epilepsy and stroke.
DC  B04 D16
IN  COX, P; DIXON, A; JACKSON, A; MORGAN, K
PA  (UYCA-N) UNIV CAMBRIDGE TECH SERVICES LTD; (WARN)
WARNER LAMBERT CO
CYC 91
PI  WO 2000063367 A1 20001026 (200064)* EN  87p  C12N015-12
      RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT
KE LS LU MC MW NL
        OA PT SD SE SL SZ TZ UG ZW
      W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU
CZ DE DK DM EE ES
        FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
LC LK LR LS
        LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO
RU SD SE SG SI SK SL
        TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
    AU 2000032851 A  20001102 (200107)          C12N015-12
    EP 1171589  A1 20020116 (200207) EN         C12N015-12
      R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL
PT SE
    JP 2002541840 W  20021210 (200301)  101p  C12N015-09
ADT WO 2000063367 A1 WO 2000-EP1783 20000224; AU
2000032851 A AU 2000-32851
    20000224; EP 1171589 A1 EP 2000-910753 20000224, WO
2000-EP1783 20000224;
    JP 2002541840 W JP 2000-612446 20000224, WO 2000-EP1783
20000224
FDT AU 2000032851 A Based on WO 2000063367; EP 1171589 A1
Based on WO
    2000063367; JP 2002541840 W Based on WO 2000063367
PRAI US 1999-129473P  19990415
IC  ICM C12N015-09; C12N015-12
    ICS A61K038-00; A61K048-00; A61P009-00; A61P009-10;
A61P025-04;
      A61P025-20; A61P025-28; A61P043-00; C07K014-47;
C07K014-705;
      C12N001-15; C12N001-19; C12N001-21; C12N005-10;
C12P021-02;
      C12Q001-02; C12Q001-68; G01N033-15; G01N033-50;
G01N033-53;
      G01N033-566; G01N033-58


=> d ibib abs l4 1-29

L4  ANSWER 1 OF 29  MEDLINE on STN              DUPLICATE 1
ACCESSION NUMBER:  2003394388  MEDLINE
DOCUMENT NUMBER:  22811917  PubMed ID: 12930796
TITLE:          Sodium channel beta4, a new disulfide-linked auxiliary
                subunit with similarity to beta2.
AUTHOR:         Yu Frank H; Westenbroek Ruth E; Silos-Santiago
Inmaculada;
                McCormick Kimberly A; Lawson Deborah; Ge Pei; Ferriera
                Holly; Lilly Jeremiah; DiStefano Peter S; Catterall William
                A; Scheuer Todd; Curtis Rory
CORPORATE SOURCE:  Department of Pharmacology, University of
Washington,
                Seattle, Washington 98195-7280, USA.
CONTRACT NUMBER:  NS25704 (NINDS)
    NS34802 (NINDS)
SOURCE:         JOURNAL OF NEUROSCIENCE, (2003 Aug 20) 23
(20) 7577-85.
                Journal code: 8102140. ISSN: 1529-2401.
PUB. COUNTRY:  United States
DOCUMENT TYPE:  Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:       English
FILE SEGMENT:  Priority Journals
ENTRY MONTH:  200309
ENTRY DATE:  Entered STN: 20030823
                Last Updated on STN: 20030924
                Entered Medline: 20030923
AB  The principal alpha subunit of  ***voltage*** - ***gated***
    ***sodium***  ***channels***  is associated with auxiliary beta
    subunits that modify channel function and mediate protein-protein
    interactions. We have identified a new beta subunit termed beta4. Like
    the beta1- ***beta3***  subunits, beta4 contains a cleaved signal
    sequence, an extracellular Ig-like fold, a transmembrane segment, and a
    short intracellular C-terminal tail. Using TaqMan reverse
    transcription-PCR analysis, in situ hybridization, and
    immunocytochemistry, we show that beta4 is widely distributed in
neurons
    in the brain, spinal cord, and some sensory neurons.beta4 is most similar
    to the beta2 subunit (35% identity), and, like the beta2 subunit, the
    Ig-like fold of beta4 contains an unpaired cysteine that may interact with
    the alpha subunit. Under nonreducing conditions, beta4 has a molecular
    mass exceeding 250 kDa because of its covalent linkage to Nav1.2a,
whereas
    on reduction, it migrates with a molecular mass of 38 kDa, similar to
the
    mature glycosylated forms of the other beta subunits. Coexpression of
    beta4 with brain Nav1.2a and skeletal muscle Nav1.4 alpha subunits in
    tsA-201 cells resulted in a negative shift in the voltage dependence of
    channel activation, which overrode the opposite effects of beta1 and
     ***beta3***  subunits when they were present. This novel,
    disulfide-linked beta subunit is likely to affect both protein-protein
    interactions and physiological function of multiple sodium channel alpha
    subunits.

L4  ANSWER 2 OF 29  MEDLINE on STN              DUPLICATE 2
ACCESSION NUMBER:  2003461549  IN-PROCESS
DOCUMENT NUMBER:  22885672  PubMed ID: 14522002
TITLE:          Expression of auxiliary beta subunits of sodium channels
in
                primary afferent neurons and the effect of nerve injury.
AUTHOR:         Takahashi N; Kikuchi S; Dai Y; Kobayashi K; Fukuoka
T;
                Noguchi K
CORPORATE SOURCE:  Department of Anatomy and Neuroscience,
Hyogo college of
                Medicine, 1-1 Mukogawa-cho, Nishinomiya City, Hyogo
                663-8501, Japan.
SOURCE:         NEUROSCIENCE, (2003) 121 (2) 441-50.
                Journal code: 7605074. ISSN: 0306-4522.
PUB. COUNTRY:  United States
DOCUMENT TYPE:  Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:       English
FILE SEGMENT:  IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE:  Entered STN: 20031003
                Last Updated on STN: 20031122
AB  Multiple  ***voltage*** - ***gated***  ***sodium***
    ***channels***  are the primary mediators of cell excitability. They
are
    multimers that consist of the pore-forming alpha subunit and auxiliary
    beta subunits. Although ion permeability and voltage sensing are
    primarily determined by the alpha subunit, beta subunits are important
    modulators of sodium channel function. The purpose of this study was
to
    assess the effect of axotomy on the expression of beta subunits (beta(1),
    beta(2) and  ***beta***  ( ***3*** )) and coexpression of Na(v)1.3
and
     ***beta***  ( ***3*** ) subunits in the dorsal root ganglion (DRG).
We
    used sciatic nerve transection models or spared nerve injury (SNI)
models
    in the rat. In reverse transcriptase-polymerase chain reaction analysis,
    there were no significant differences between contralateral and
    ipsilateral DRGs of beta(1) and beta(2) mRNA 3 days after axotomy.
     ***beta***  ( ***3*** ) mRNA expression in ipsilateral DRGs
increased
    significantly compared with contralateral DRGs 3 days after axotomy.
In
    in situ hybridization histochemistry, beta(1) mRNA was predominantly
    expressed in medium- to large-size neurons, whereas beta(2) mRNA
was
    expressed in small- to large-size neurons. There were no significant
    differences in beta(1) and beta(2) mRNA between contralateral and
    ipsilateral DRGs 3 days after axotomy. In contrast,  ***beta***  (
     ***3*** ) mRNA was mainly expressed in small neurons and
occasionally in
    medium- to large-size neurons, and  ***beta***  ( ***3*** ) mRNA
    expression in small c-type neurons in ipsilateral DRGs was increased
    significantly compared with contralateral DRGs. We examined
***beta***
    ( ***3*** ) mRNA expression with one of alpha subunits, Na(v)1.3-ir,
in
    DRG neurons after axotomy using the double labeling method. We
found a
    high percentage of coexpression in injured DRG neurons: 83.6+/-2.8%
of
    neurons expressing  ***beta***  ( ***3*** ) mRNA were labeled for
    Na(v)1.3-ir; 70.1+/-3.1% of Na(v)1.3-ir neurons expressed
***beta*** (
     ***3*** ) mRNA. We also examined the expression of  ***beta***
(
     ***3*** ) mRNA in DRG neurons in the SNI model, a neuropathic
pain model.
    We used activating transcription factor 3 to identify axotomized
neurons,
    and found that  ***beta***  ( ***3*** ) mRNA up-regulation
occurred
    mainly in axotomized neurons in the neuropathic pain model. These
data
    strongly suggest that  ***beta***  ( ***3*** ) expression in injured
    DRG neurons following axotomy might be an important
pathomechanism of
    post-nerve injury pain in primary sensory neurons.

L4  ANSWER 3 OF 29  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:  2003:484037  CAPLUS
DOCUMENT NUMBER:  139:211199
TITLE:          Expression and distribution of  ***voltage*** -
                ***gated***  ***sodium***  ***channels***  in
                the cerebellum
AUTHOR(S):      Schalter, Kristin L.; Caldwell, John H.
CORPORATE SOURCE:  Department of Cellular and Structural
Biology,
                University of Colorado Health Sciences Center, Denver,
                CO, USA
SOURCE:         Cerebellum (2003), 2(1), 2-9
                CODEN: CEREC9; ISSN: 1473-4222
PUBLISHER:      Taylor & Francis Ltd.
DOCUMENT TYPE:  Journal; General Review
LANGUAGE:       English
AB  A review. In order to understand the effects of Na+ channels on
synaptic
    signaling and response in the cerebellum, it is essential to know for each
    class of neuron which Na+ channel isoforms are present, and the
properties
    and distribution of each. Na+ channels are heteromultimeric membrane
    proteins, consisting of a large .alpha. subunit that forms the pore, and
    one or more .beta. subunits. Ten genes encode an .alpha. subunit in
    mammals, and of these, 4 are expressed in the cerebellum: NaV1.1,
NaV1.2,
    NaV1.3, and NaV1.6. Three genes encode .beta. subunits
(Na.beta.1-3), and
    all 3 are expressed in the cerebellum. However, NaV1.3 and Na.
     ***beta*** . ***3***  have been found only in the developing
    cerebellum. All Na+ channels recorded in the cerebellum are
TTX-sensitive
    with similar kinetics, making it difficult to identify the isoforms elec.
    Thus, most of the expression studies have relied on techniques that
allow
    visualization of Na+ channel subtypes at the level of mRNA and
protein.
    In situ hybridization and immunolocalization studies have demonstrated
    that granule cells predominantly express NaV1.2, NaV1.6, Na.beta.1,
and
    Na.beta.2. Protein for NaV1.2 and NaV1.6 is localized primarily in
    granule cell parallel fibers. Purkinje cells express NaV1.1, NaV1.6,
    Na.beta.1, and Na.beta.2. The somato-dendritic localization of NaV1.1
and
    NaV1.6 in Purkinje cells suggests that these isoforms are involved in the
    integration of synaptic input. Deep cerebellar nuclei neurons express
    NaV1.1 and NaV1.6 as well as Na.beta.1. Bergmann glia express
NaV1.6, but
    not granule cell layer astrocytes. Some Na+ channel isoforms that are
not
    expressed normally in the adult cerebellum are expressed in animals
with
    mutations or disease. Electrophysiol. studies suggest that NaV1.6 is
    responsible for spontaneous firing and bursting features in Purkinje
    cells, but the specialized functions of the other subunits in the
    cerebellum remain unknown.
REFERENCE COUNT:  60  THERE ARE 60 CITED
REFERENCES AVAILABLE FOR THIS
                RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L4  ANSWER 4 OF 29  WPIDS  COPYRIGHT 2003 THOMSON
DERWENT on STN
ACCESSION NUMBER:  2002-627599 [67]  WPIDS
CROSS REFERENCE:  2003-787079 [74]
DOC. NO. CPI:  C2002-177169
TITLE:          New transgenic animal line, useful for identifying or
                isolating pure populations of cells useful for
                pharmacological, behavioral, electrophysiological, gene
                expression, drug discovery, or target validation assays.
DERWENT CLASS:  B04 D16 P14
INVENTOR(S):  SERAFINI, T A
PATENT ASSIGNEE(S):  (SERA-I) SERAFINI T A; (RENO-N)
RENOVIS INC
COUNTRY COUNT:  100
PATENT INFORMATION:

  PATENT NO  KIND DATE  WEEK  LA  PG
  ---------------------------------
  WO 2002064749 A2 20020822 (200267)* EN  170
    RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT
KE LS LU MC MW MZ
      NL OA PT SD SE SL SZ TR TZ UG ZM ZW
    W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN
CO CR CU CZ DE DK
      DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP
KE KG KP KR
      KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ
NO NZ OM PH PL PT
      RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US
UZ VN YU ZA ZM
      ZW
  US 2003051266 A1 20030313 (200321)

APPLICATION DETAILS:

  PATENT NO  KIND  APPLICATION  DATE
  ---------------------------------
  WO 2002064749 A2  WO 2002-US4765  20020214
  US 2003051266 A1  US 2001-783487  20010214


PRIORITY APPLN. INFO: US 2001-783487  20010214
AN  2002-627599 [67]  WPIDS
CR  2003-787079 [74]
AB  WO 200264749 A UPAB: 20031117
    NOVELTY - A collection of lines at least 5 transgenic animals having a
    transgene comprising:
```

(a) a sequence coding for a selectable or detectable marker protein, or for an activator or repressor of expression of a second nucleotide sequence encoding a detectable/selectable marker; and

(b) regulatory sequences of a characterizing gene corresponding to an endogenous gene or ortholog (the transgene is at a site in the genome other than where the endogenous gene is located).

DETAILED DESCRIPTION - A collection of lines at least 5 transgenic animals having a transgene comprising:

(a) a sequence coding for a selectable or detectable marker protein, or for an activator or repressor of expression of a second nucleotide sequence encoding a detectable/selectable marker; and

(b) regulatory sequences of a characterizing gene corresponding to an endogenous gene or ortholog (the transgene is at a site in the genome other than where the endogenous gene is located).

The regulatory sequences are operably linked to the first nucleotide sequence which is expressed in the transgenic animal in a similar pattern to that of the endogenous gene in a comparable non-transgenic animal or its anatomical region (the characterizing gene is different for each of the transgenic animals).

INDEPENDENT CLAIMS are also included for:

(1) a method of making a collection of lines of transgenic animals, comprising:

(a) introducing into the genome of a founder animal the above transgene;

(b) breeding the founder animal to produce a line of transgenic animals; and

(c) repeating steps (a) and (b) four or more times, each time with a different characterizing gene to generate four or more additional lines of transgenic animals, to generate a collection of lines of transgenic animals;

(2) a collection of vectors for making transgenic animals, which comprises 5 or more of vectors comprising the above transgene;

(3) a method of making a collection of vectors for making transgenic animals, comprising:

(a) constructing a vector comprising the transgene; and

(b) repeating step (a) four more times (each time step (a) is repeated a different characterizing gene is used to generate a collection of vectors for making transgenic animals);

(4) a transgenic animal comprising 2 or more of the above transgenes;

(5) a method of isolating a collection of pure populations of cells having at least 2 different populations of cells, comprising isolating from 3 or more transgenic animals from the collection of transgenic animals, the cells expressing the selectable or detectable marker from cells not expressing the selectable or detectable marker;

(6) a collection of pure populations of cells isolated from the transgenic animals of the above collection (cells express the detectable or selectable marker and each of the pure populations is isolated from a transgenic animal having a different characterizing gene); and

(7) methods of screening a candidate molecule for an effect on one or more cell types, comprising:

(a) contacting the molecule to cells from each pure population of cells in the collection; and

(b) detecting a change in cells from each of the pure population in response to the step of contacting (detecting a change in cells in response to contacting indicates that the candidate molecule has an effect on one or more of the cell types); or

(c) administering the candidate molecule to a transgenic animal from each line of the collection;

(d) isolating a pure population of cells from each of the transgenic animals that express the first nucleotide sequence from the cells that do not express the sequence; and

(e) detecting a change in the pure populations of cells from the transgenic animals administered the candidate molecule in comparison to those are not administered the candidate molecule (detecting a change in the cells in response to the step of contacting indicates that the molecule has an effect on one or more of the cell types).

USE - The transgenic animal lines are useful for identifying or isolating pure populations of particular classes of cells which may be used for pharmacological, behavioral, electrophysiological, gene expression, drug discovery, or target validation assays. The methods and vectors are useful for producing the transgenic animal lines.

Dwg.0/3

L4 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:937303 CAPLUS
DOCUMENT NUMBER: 138:20443
TITLE: Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes
INVENTOR(S): Kondo, Akihiro; Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto, Yoshimasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunoshin
PATENT ASSIGNEE(S): Takara Bio Inc., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 386 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002355079	A2	20021210	JP 2002-69354	20020313
PRIORITY APPLN. INFO.:			JP 2001-73183	A 20010314
			JP 2001-74993	A 20010315
			JP 2001-102519	A 20010330

AB A method and kit for detecting endocrine-disrupting chems. using DNA microarrays are claimed. The method comprises prepg. a nucleic acid sample contg. mRNAs or cDNAs originating in cells, tissues, or organisms which have been brought into contact with a sample contg. the endocrine disruptor. The nucleic acid sample is hybridized with DNA microarrays having genes affected by the endocrine disruptor or DNA fragments originating in these genes have been fixed. The results obtained are then compared with the results obtained with the control sample to select the gene affected by the endocrine disruptor. Genes whose expression is altered by tri-Bu tin, 4-octaphenol, 4-nonylphenol, di-N-Bu phthalate, dichlorohexyl phthalate, octachlorostyrene, benzophenone, diethylhexyl phthalate, diethylstilbestrol (DES), and 17-.beta. estradiol (E2), were found in mice by DNA chip anal.

L4 ANSWER 6 OF 29 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2002462405 MEDLINE
DOCUMENT NUMBER: 22209864 PubMed ID: 12220575
TITLE: Functional modulation of human brain Nav1.3 sodium channels, expressed in mammalian cells, by auxiliary beta 1, beta 2 and ***beta*** ***3*** subunits.
AUTHOR: Meadows L S; Chen Y H; Powell A J; Clare J J; Ragsdale D S
CORPORATE SOURCE: Montreal Neurological Institute, McGill University, Montreal, QC, Canada.
SOURCE: NEUROSCIENCE, (2002) 114 (3) 745-53.
Journal code: 7605074. ISSN: 0306-4522.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20020911
Last Updated on STN: 20021221
Entered Medline: 20021220
AB ***Voltage*** - ***gated*** ***sodium*** ***channels*** consist of a pore-forming alpha subunit and two auxiliary beta subunits. Excitable cells express multiple alpha subtypes, designated Na(v)1.1-Na(v)1.9, and three beta subunits, designated beta1, beta2 and ***beta3*** . Understanding how the different alpha subtypes, in combination with the various beta subunits, determine sodium channel behavior is important for elucidating the molecular basis of sodium channel functional diversity. In this study, we used whole-cell electrophysiological recording to examine the properties of the human Na(v)1.3 alpha subtype, stably expressed in Chinese hamster ovary cells, and to investigate modulation of Na(v)1.3 function by beta1, beta2 and ***beta3*** subunits. In the absence of beta subunits, human Na(v)1.3 formed channels that inactivated rapidly (tau(inactivation) approximately equals 0.5 ms at 0 mV) and almost completely by the end of 190-ms-long depolarizations. Using an intracellular solution with aspartate as the main anion, the midpoint for channel activation was approximately -12 mV. The midpoint for inactivation, determined using 100-ms conditioning pulses, was approximately -47 mV. The time constant for repriming of inactivated channels at -80 mV was approximately 6 ms. Coexpression of beta1 or ***beta3*** did not affect inactivation time course or the voltage dependence of activation, but shifted the inactivation curve approximately 10 mV negative, and slowed the repriming rate ca. three-fold. beta2 did not affect channel properties, either by itself or in combination with beta1 or ***beta3*** . Na(v)1.3 expression is increased in damaged nociceptive peripheral afferents. This change in channel expression levels is correlated with the emergence of a rapidly inactivating and rapidly repriming sodium current, which has been proposed to contribute to the pathophysiology of neuropathic pain. The results of this study support the hypothesis that Na(v)1.3 may mediate this fast sodium current.
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L4 ANSWER 7 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 4
ACCESSION NUMBER: 2003:166406 BIOSIS
DOCUMENT NUMBER: PREV200300166406
TITLE: Contrasting functions of the extracellular and intracellular domains of the ***voltage*** - ***gated*** ***sodium*** ***channel*** subunit NaVbeta3.1.
AUTHOR(S): Havard, A. C. [Reprint Author]; Morgan, K.; Yu, E. J. [Reprint Author]; Russell, M. [Reprint Author]; Jackson, A. P. [Reprint Author]
CORPORATE SOURCE: Department of Biochemistry, University of Cambridge, Cambridge, UK
SOURCE: Molecular Biology of the Cell, (Nov. 2002) Vol. 13, No. Supplement, pp. 220a. print.
Meeting Info.: 42nd Annual Meeting of the American Society for Cell Biology. San Francisco, CA, USA. December 14-18, 2002. American Society for Cell Biology.
CODEN: MBCEEV. ISSN: 1059-1524.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Apr 2003
Last Updated on STN: 2 Apr 2003

L4 ANSWER 8 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:380250 BIOSIS
DOCUMENT NUMBER: PREV200300380250
TITLE: PUTATIVE CYSTEINE RESIDUES RESPONSIBLE FOR DISULFIDE LINKAGE OF SODIUM CHANNEL NAV1.2 alpha SUBUNITS TO THE beta2 SUBUNIT.
AUTHOR(S): Davis, T. H. [Reprint Author]; Isom, L. L. [Reprint Author]
CORPORATE SOURCE: Department of Pharmacology, Univ. of Michigan, Ann Arbor, MI, USA
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2002) Vol. 2002, pp. Abstract No. 835.6. http://sfn.scholarone.com. cd-rom.
Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience. Orlando, Florida, USA. November 02-07, 2002. Society for Neuroscience.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Aug 2003
Last Updated on STN: 20 Aug 2003
AB ***Voltage*** - ***gated*** ***sodium*** ***channels*** are composed of a pore forming alpha subunit and one or two auxiliary beta subunits (beta 1,beta 2, ***beta*** ***3*** , or beta 1A) that modulate the ion conducting properties of the channel as well as channel density in the plasma membrane. Sodium channel beta subunits are also cell adhesion molecules of the immunoglobulin superfamily. beta 1, beta 1A, and ***beta*** ***3*** subunits are non-covalently associated with alpha, while beta 2 subunits are disulfide linked to the alpha subunit. Using site directed mutagenesis, we individually mutated each of the cysteine residues in beta 2 to alanine (with exception to those comprising the immunoglobulin loop) and examined their role in disulfide linkage to Nav1.2 alpha subunits. Examination of mutant beta 2 association with Nav1.2 was conducted using a combination of immunoprecipitations from stably transfected 1610 Chinese hamster lung cell lines, two microelectrode voltage clamp in oocytes, as well as cell surface saxitoxin binding.

L4 ANSWER 9 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:326317 BIOSIS
DOCUMENT NUMBER: PREV200300326317
TITLE: REGULATION OF SODIUM CHANNEL GENE EXPRESSION BY NGF IN PITUITARY GH3 CELLS.
AUTHOR(S): Espinosa-Perez, J. L. [Reprint Author]; Lopez-Dominguez, A. M. [Reprint Author]; Vega, A. V. [Reprint Author]; Navarrete, A. [Reprint Author]; Cota, G. [Reprint Author]
CORPORATE SOURCE: Dept. of Physiology, Biophysics and Neurosciences, Cinvestav-IPN, Mexico, DF, Mexico
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2002) Vol. 2002, pp. Abstract No. 743.3. http://sfn.scholarone.com. cd-rom.
Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience. Orlando, Florida, USA. November 02-07, 2002. Society for Neuroscience.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jul 2003
Last Updated on STN: 16 Jul 2003
AB There is increasing evidence that nerve growth factor (NGF) is an autocrine differentiation factor for anterior pituitary lactotropes. Because the secretory activity of these cells is under the control of spontaneous Ca2+ and Na+ action potentials, we are studying the effects of NGF on the function and expression of lactotrope ion channels. Here, we report that this growth factor promotes the expression of voltage-gated Na+ channels in the lactosomatotrope cell line GH3, which is known to be committed by NGF to acquire a lactotrope-like phenotype. Total RNA was isolated from control GH3 cells and cells that were exposed to exogenous NGF (50 ng/ml) for 3-4 days. RNA samples were then subjected to semi-quantitative RT-PCR using primers specific for mRNAs encoding Na+ channel subunits. NGF treatment induced 70-100% elevations in the mRNAs for Nav1.2 and Nav1.3 without altering transcript levels for Nav1.1, Nav1.6, beta1 and ***beta3*** subunits. Significant levels of beta2 mRNA could not be detected in control or NGF-treated cells. The NGF-induced upregulation of Nav1.2 and Nav1.3 mRNAs was accompanied by a 2-fold increase in whole-cell Na+ current density, as revealed by patch-clamp experiments. Finally, when NGF was applied in combination with 1.0 M nimodipine (a blocker of L-type Ca2+ channels), the mRNAs for Nav1.2 and Nav1.3 decreased to a low level that was not significantly different of that observed in cells that were treated with nimodipine alone. Thus, in response to NGF, GH3 cells exhibit an increased expression of two different Na+ channel isoforms, and the activation of

L-type Ca2+ channels is required for this response.

L4 ANSWER 10 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:268469 BIOSIS
DOCUMENT NUMBER: PREV200300268469
TITLE: EXPRESSION OF AUXILIARY SUBUNITS OF SODIUM CHANNEL IN SPINAL SENSORY NEURONS AND THE EFFECT OF AXOTOMY.
AUTHOR(S): Takahashi, N. [Reprint Author]; Kikuchi, S.; Noguchi, K. [Reprint Author]
CORPORATE SOURCE: Anat. and Neurosci., Hyogo Col. of Med., Nishinomiya, Japan
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2002) Vol. 2002, pp. Abstract No. 50.10. http://sfn.scholarone.com. cd-rom.
Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience. Orlando, Florida, USA. November 02-07, 2002.
Society for Neuroscience.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jun 2003
Last Updated on STN: 11 Jun 2003
AB Multiple ***voltage*** - ***gated*** ***sodium*** ***channels*** are the primary mediators of cell excitability. They are multimers that consist of the pore-forming alpha subunit and auxiliary beta subunits. Although ion permeability and voltage sensing are primarily determined by the alpha subunit, beta subunits are important modulators of sodium channel function. The purpose of this study is to assess the expression of the auxiliary beta subunits (beta1, beta2 and ***beta3***) in DRG neuron and the effect of peripheral axotomy. Male SD rats (250-300 g) received an unilateral sciatic nerve transection and were sacrificed three or seven days after axotomy. In RT-PCR analysis, there were no significant differences between contralateral and ipsilateral DRGs of beta1 and beta2 mRNAs three days after axotomy. ***beta3*** mRNA expression in ipsilateral DRGs increased significantly compared with contralateral DRGs. In in situ hybridization histochemistory, beta1 and beta2 mRNAs were predomominantly expressed in large to medium-sized neurons, and there were no significant differences between contralateral and ipsilateral DRGs three or seven days after axotomy. In contrast, ***beta3*** mRNAs was mainly expressed in small neurons and occasionally in large to medium-sized neurons, and we found that ***beta3*** mRNA expression in small c-type neurons in ipsilateral DRGs was increased significantly compared with contralateral. There were no significant increase in ***beta3*** mRNA expression in large to medium-sized neurons between contralateral and ipsilateral DRGs. These data suggest that ***beta3*** subunit may be more important modulators of sodium channel function following axotomy compared with beta1 and beta2 subunits.

L4 ANSWER 11 OF 29 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001442932 MEDLINE
DOCUMENT NUMBER: 21380269 PubMed ID: 11487618
TITLE: Nav1.3 sodium channels: rapid repriming and slow closed-state inactivation display quantitative differences after expression in a mammalian cell line and in spinal sensory neurons.
AUTHOR: Cummins T R; Aglieco F; Renganathan M; Herzog R I; Dib-Hajj S D; Waxman S G
CORPORATE SOURCE: Department of Neurology and Paralyzed Veterans of America/Eastern Paralyzed Veterans Association Neuroscience Research Center, Yale Medical School, New Haven, Connecticut 06510, USA.
SOURCE: JOURNAL OF NEUROSCIENCE, (2001 Aug 15) 21 (16) 5952-61.
Journal code: 8102140. ISSN: 1529-2401.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20010903
Entered Medline: 20010830
AB Although rat brain Nav1.3 ***voltage*** - ***gated*** ***sodium*** ***channels*** have been expressed and studied in Xenopus oocytes, these channels have not been studied after their expression in mammalian cells. We characterized the properties of the rat brain Nav1.3 sodium channels expressed in human embryonic kidney (HEK) 293 cells. Nav1.3 channels generated fast-activating and fast-inactivating currents. Recovery from inactivation was relatively rapid at negative potentials (<-80 mV) but was slow at more positive potentials. Development of closed-state inactivation was slow, and, as predicted on this basis, Nav1.3 channels generated large ramp currents in response to slow depolarizations. Coexpression of ***beta3*** subunits had small but significant effects on the kinetic and voltage-dependent properties of Nav1.3 currents in HEK 293 cells, but coexpression of beta1 and beta2 subunits had little or no effect on Nav1.3 properties. Nav1.3 channels, mutated to be tetrodotoxin-resistant (TTX-R), were expressed in SNS-null dorsal root ganglion (DRG) neurons via biolistics and were compared with the same construct expressed in HEK 293 cells. The voltage dependence of steady-state inactivation was approximately 7 mV more depolarized in SNS-null DRG neurons, demonstrating the importance of background cell type in determining physiological properties. Moreover, consistent with the idea that cellular factors can modulate the properties of Nav1.3, the repriming kinetics were twofold faster in the neurons than in the HEK 293 cells. The rapid repriming of Nav1.3 suggests that it contributes to the acceleration of repriming of TTX-sensitive (TTX-S) sodium currents that are seen after peripheral axotomy of DRG neurons. The relatively rapid recovery from inactivation and the slow closed-state inactivation kinetics of Nav1.3 channels suggest that neurons expressing Nav1.3 may exhibit a reduced threshold and/or a relatively high frequency of firing.

L4 ANSWER 12 OF 29 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN DUPLICATE 6
ACCESSION NUMBER: 2002:73581 SCISEARCH
THE GENUINE ARTICLE: 511PH
TITLE: Developmental expression of the novel ***voltage*** - ***gated*** ***sodium*** ***channel*** auxiliary subunit ***beta*** ***3*** in rat CNS (vol 534, pg 763, 2001)
AUTHOR: Shah B S (Reprint); Stevens E B; Pinnock R D; Dixon A K; Lee K
SOURCE: JOURNAL OF PHYSIOLOGY-LONDON, (15 DEC 2001) Vol. 537, No. 3, pp. 1073-1074.
Publisher: CAMBRIDGE UNIV PRESS, 40 WEST 20TH ST, NEW YORK, NY 10011-4221 USA.
ISSN: 0022-3751.
DOCUMENT TYPE: Errata; Journal
LANGUAGE: English
REFERENCE COUNT: 1

L4 ANSWER 13 OF 29 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2001437841 MEDLINE
DOCUMENT NUMBER: 21376386 PubMed ID: 11483707
TITLE: Developmental expression of the novel ***voltage*** - ***gated*** ***sodium*** ***channel*** auxiliary subunit ***beta3*** , in rat CNS.
COMMENT: Erratum in: J Physiol 2001 Dec 15;537(Pt 3):1073-4
AUTHOR: Shah B S; Stevens E B; Pinnock R D; Dixon A K; Lee K
CORPORATE SOURCE: Parke Davis Neuroscience Research Centre, Cambridge University Forvie Site, Cambridge CB2 2QB, UK.
SOURCE: JOURNAL OF PHYSIOLOGY, (2001 Aug 1) 534 (Pt 3) 763-76.
Journal code: 0266262. ISSN: 0022-3751.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20011008
Last Updated on STN: 20020320
Entered Medline: 20011004
AB 1. We have compared the mRNA distribution of sodium channel alpha subunits known to be expressed during development with the known auxiliary subunits Nabeta1.1 and Nabeta2.1 and the novel, recently cloned subunit, ***beta3*** . 2. In situ hybridisation studies demonstrated high levels of Nav1.2, Nav1.3, Nav1.6 and ***beta3*** mRNA at embryonic stages whilst Nabeta1.1 and Nabeta2.1 mRNA was absent throughout this period. 3. Nabeta1.1 and Nabeta2.1 expression occurred after postnatal day 3 (P3), increasing steadily in most brain regions until adulthood. ***beta3*** expression differentially decreased after P3 in certain areas but remained high in the hippocampus and striatum. 4. Emulsion-dipped slides showed co-localisation of ***beta3*** with Nav1.3 mRNA in areas of the CNS suggesting that these subunits may be capable of functional interaction. 5. Co-expression in Xenopus oocytes revealed that ***beta3*** could modify the properties of Nav1.3; ***beta3*** changed the equilibrium of Nav1.3 between the fast and slow gating modes and caused a negative shift in the voltage dependence of activation and inactivation. 6. In conclusion, ***beta3*** is shown to be the predominant beta subunit expressed during development and is capable of modulating the kinetic properties of the embryonic Nav1.3 subunit. These findings provide new information regarding the nature and properties of ***voltage*** - ***gated*** ***sodium*** ***channels*** during development.

L4 ANSWER 14 OF 29 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2001257066 MEDLINE
DOCUMENT NUMBER: 21079735 PubMed ID: 11212211
TITLE: Tissue distribution and functional expression of the human ***voltage*** - ***gated*** ***sodium*** ***channel*** ***beta3*** subunit.
AUTHOR: Stevens E B; Cox P J; Shah B S; Dixon A K; Richardson P J; Pinnock R D; Lee K
CORPORATE SOURCE: Parke-Davis Neuroscience Research Centre, Cambridge University, UK.
SOURCE: PFLUGERS ARCHIV. EUROPEAN JOURNAL OF PHYSIOLOGY, (2001 Jan) 441 (4) 481-8.
Journal code: 0154720. ISSN: 0031-6768.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010521
Last Updated on STN: 20010521
Entered Medline: 20010517
AB This study investigated the distribution of ***beta3*** in human tissues and the functional effects of the human ***beta3*** subunit on the gating properties of brain and skeletal muscle alpha subunits. Using RT-PCR of human cDNA panels, ***beta3*** message was detected in brain, heart, kidney, lung, pancreas and skeletal muscle. Both alphaIIA and SkM1 expressed in Xenopus oocytes inactivated with a time course described by two exponential components representing fast and slow gating modes, while co-expression of human ***beta3*** with alphaIIA or SkM1 significantly increased the proportion of channels operating by the fast gating mode. In the presence of ***beta3*** a greater proportion of alphaIIA or SkM1 current was described by the fast time constant for both inactivation and recovery from inactivation. ***beta3*** caused a hyperpolarizing shift in the voltage dependence of inactivation of alphaIIA and reduced the slope factor. The voltage dependence of inactivation of SkM1 was described by a double Boltzmann equation. However, SkM1 co-expressed with ***beta3*** was described by a single Boltzmann equation similar to one of the Boltzmann components for SkM1 expressed alone, with a small positive shift in V1/2 value and reduced slope factor. This is the first study demonstrating that ***beta3*** is expressed in adult mammalian skeletal muscle and can functionally couple to the skeletal muscle alpha subunit, SkM1.

L4 ANSWER 15 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:487058 BIOSIS
DOCUMENT NUMBER: PREV200100487058
TITLE: The ***voltage*** - ***gated*** ***sodium*** ***channel*** ***beta3*** subunit up-regulates functional sensory neuron specific (SNS) alpha-subunit expression in recombinant mammalian cells.
AUTHOR(S): Powell, A. J. [Reprint author]; Sidhu, H. S. [Reprint author]; John, V. H. [Reprint author]; Hick, C. A. [Reprint author]; Grose, D. T. [Reprint author]; Gladwell, Z. M. [Reprint author]; Plumpton, C.; Kinghorn, I. J.; Jowett, A.; Pratt, G. D.; Main, M. J. [Reprint author]; Trezise, D. J. [Reprint author]; Clare, J. J. [Reprint author]; Tate, S. N. [Reprint author]
CORPORATE SOURCE: Molecular Pharmacology Dept., GlaxoSmithKline R and D, Stevenage, UK
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 116. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience. San Diego, California, USA. November 10-15, 2001.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Oct 2001
Last Updated on STN: 23 Feb 2002
AB ***Voltage*** - ***gated*** ***sodium*** ***channels*** comprise a large pore-forming alpha-subunit that may be associated with one or two of the three known auxiliary beta-subunits (beta1, beta2 and ***beta3***). The beta-subunits modulate the voltage-dependence and kinetic properties of the alpha-subunits with which they associate and are believed to facilitate localisation of the channel to specific membranes. Differential expression of distinct sodium channel alpha-subunit and beta-subunit subtypes contributes to the distinct electrophysiological characteristics of different neuronal membranes. We show that the ***beta3*** -subunit is expressed in human DRG. Co-expression of the human ***beta3*** -subunit with the human SNS/Nav1.8 alpha-subunit in Xenopus oocytes gives approximately a 2.5 fold increase in peak current amplitude. Co-expression of SNS alpha and ***beta3*** in

mammalian
cells gives approximately a 6-fold increase in peak current amplitude and
a 5 mV negative shift in the voltage-dependence of channel activation. ***beta3*** -mediated up-regulation of SNS currents may contribute to
increased excitability in DRG neurons. We have generated and characterised stable cell lines expressing SNS alpha alone, ***beta3***
alone and co-expressing the SNS alpha+ ***beta3*** subunits. These
cell lines (along with stable cell lines expressing beta1 and beta2) have been used to validate beta1, beta2 and ***beta3*** -subunit-specific affinity purified rabbit antibodies.

L4 ANSWER 16 OF 29 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2001444189 MEDLINE
DOCUMENT NUMBER: 21382838 PubMed ID: 11489532
TITLE: ***Beta3*** , a novel auxiliary subunit for the ***voltage*** ***gated*** ***sodium*** ***channel*** is upregulated in sensory neurones following streptozocin induced diabetic neuropathy in rat.
AUTHOR: Shah B S; Gonzalez M I; Bramwell S; Pinnock R D; Lee K; Dixon A K
CORPORATE SOURCE: Pfizer Global Research and Development, Cambridge Laboratories, Cambridge University Forvie Site, Robinson Way, CB2 2QB, Cambridge, UK.
SOURCE: NEUROSCIENCE LETTERS, (2001 Aug 17) 309 (1) 1-4.
Journal code: 7600130. ISSN: 0304-3940.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20011001
Entered Medline: 20010927
AB In the present study we have used in situ hybridization to examine the changes in mRNA expression of the ***voltage*** ***gated*** ***sodium*** ***channel*** subunits beta1 and ***beta3*** , which
occur in response to streptozocin induced diabetic neuropathy. Under control conditions beta1 mRNA was detected throughout the spinal cord and
in large dorsal root ganglion (DRG) Abeta fibres whilst ***beta3*** mRNA was expressed exclusively in the layers I/II and X of the spinal cord
and in small DRG c-fibres. Following streptozocin treatment, the expression of beta1 mRNA remained unchanged in both the spinal cord and
DRG whilst ***beta3*** message was significantly increased in both the
spinal cord and in medium diameter Adelta type DRG neurones. In conclusion, the present study illustrates that the development of the neuropathic pain state is associated with distinct changes in the pattern of ***beta3*** subunit expression and that these changes appear to be
specific to the neuropathic pain state induced.

L4 ANSWER 17 OF 29 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 10
ACCESSION NUMBER: 2000-665241 [64] WPIDS
DOC. NO. CPI: C2000-201571
TITLE: Novel nucleic acids encoding a ***beta*** - ***3*** subunit from a ***voltage*** - ***gated*** ***sodium*** ***channel*** , and their corresponding polypeptides, useful for detecting and treating sodium channel-associated conditions, e.g. pain, epilepsy and stroke.
DERWENT CLASS: B04 D16
INVENTOR(S): COX, P; DIXON, A; JACKSON, A; MORGAN, K
PATENT ASSIGNEE(S): (UYCA-N) UNIV CAMBRIDGE TECH SERVICES LTD; (WARN) WARNER LAMBERT CO
COUNTRY COUNT: 91
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000063367	A1	20001026	(200064)*	EN	87

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES
FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS
LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL
TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000032851 A 20001102 (200107)
EP 1171589 A1 20020116 (200207) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002541840 W 20021210 (200301) 101

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000063367	A1	WO 2000-EP1783	20000224
AU 2000032851	A	AU 2000-32851	20000224
EP 1171589	A1	EP 2000-910753	20000224
		WO 2000-EP1783	20000224
JP 2002541840	W	JP 2000-612446	20000224
		WO 2000-EP1783	20000224

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000032851	A Based on	WO 2000063367
EP 1171589	A1 Based on	WO 2000063367
JP 2002541840	W Based on	WO 2000063367

PRIORITY APPLN. INFO: US 1999-129473P 19990415
AN 2000-665241 [64] WPIDS
AB WO 200063367 A UPAB: 20001209
NOVELTY - Nucleic acid (I) encoding a ***beta*** ***3*** subunit
from a ***voltage*** - ***gated*** ***sodium*** ***channel***
(VGNaC), or its complement, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
following:
(1) a polynucleotide (II) comprising at least 10 consecutive nucleotides of a nucleic acid encoding a ***beta*** ***3*** subunit of a VGNaC;
(2) amplification of a ***beta*** ***3*** subunit nucleic acid comprising contacting a test sample (TS) with amplification reaction
reagents comprising a pair of primers which hybridize to (I) or (II), and optionally detecting the amplification products;
(3) a kit for the amplification of a ***beta*** ***3*** subunit nucleotide sequence comprising a pair of primers which hybridize
to (I) or (II), and optionally, amplification reagents;
(4) detecting (I) or (II) comprising contacting a TS with a probe or probes that hybridize under stringent conditions to (I) or (II), and detecting hybrid complex formation;
(5) a kit for detecting (I) or (II) comprising a probe or probes that hybridize under stringent conditions to (I) or (II), and (optionally) hybridization reagents;
(6) a recombinant vector comprising a nucleic acid as in (I) or (II);
(7) a recombinant host cell comprising a nucleic acid as in (I) or (II);
(8) producing a polypeptide encoded by (I) or (II) comprising culturing a host cell as in (8), harvesting the culture medium or lyzing the host cell, and separating or purifying the protein from the medium of the lysate;
(9) a polypeptide comprising at least a fragment of the amino acid sequence of the ***beta*** ***3*** subunit from a VGNaC;
(10) a polypeptide comprising a sequence with at least 90 % identity to at least a fragment of 1 of 2 sequences ((aa1) or (aa2)) of 215 amino acids (aa), given in the specification;
(11) a polypeptide encoded by (I) or (II);
(12) a polypeptide comprising a 1 of 30 sequences of 5-159 aa, given
in the specification;
(13) screening for ligand substances or molecules that modulate the biological activity of a VGNaC containing a ***beta*** ***3*** subunit comprising:
(a) contacting a recombinant host cell co-expressing at least a fragment of a ***beta*** ***3*** subunit and at least a fragment of a functional alpha subunit (preferably an alpha 2 subunit) of a VGNaC,
with a TS; and
(b) measuring an electrical parameter within the host cell by a voltage clamp technique or measurement of membrane potential by voltage
sensitive fluorescent dyes; and
(14) screening ligand substances or molecules that are able to modulate the biological activity of a VGNaC containing a ***beta*** ***3*** subunit comprising:
(a) contacting the ligand with at least a fragment of a ***beta*** ***3*** subunit;
(b) contacting the medium the ligand and ***beta*** ***3*** subunit containing medium with a ***beta*** ***3*** substrate; and
(c) measuring the eventual binding of the substrate to the ***beta*** ***3*** protein (fragment).
ACTIVITY - Analgesic; anticonvulsant; cerebroprotective; vasotropic;
cardiant; nootropic; cytostatic; dermatological.
MECHANISM OF ACTION - Gene therapy.
USE - The methods are useful for screening for agonists and antagonists of sodium channels. The agonists, antagonists, proteins and nucleic acids may be used diagnosing of treating diseases or conditions associated with VGNaC's. e.g. pain, epilepsy, stroke, ischemia, heart disease, Jacobsen Syndrome, Familial Nonchromaffin Paraganglioma, Phenylketonuria due to PTS deficiency and Charcot Marie Tooth disease.
Dwg.0/7

L4 ANSWER 18 OF 29 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2001060650 MEDLINE
DOCUMENT NUMBER: 20521560 PubMed ID: 11069594
TITLE: ***beta3*** , a novel auxiliary subunit for the ***voltage*** - ***gated*** ***sodium*** ***channel*** , is expressed preferentially in sensory neurons and is upregulated in the chronic constriction injury model of neuropathic pain.
AUTHOR: Shah B S; Stevens E B; Gonzalez M I; Bramwell S; Pinnock R D; Lee K; Dixon A K
CORPORATE SOURCE: Parke-Davis Neuroscience Research Centre, Cambridge University Forvie Site, Robinson Way, Cambridge CB2 2QB, UK.
SOURCE: EUROPEAN JOURNAL OF NEUROSCIENCE, (2000 Nov) 12 (11) 3985-90.
Journal code: 8918110. ISSN: 0953-816X.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001222
AB Adult dorsal root ganglia (DRG) have been shown to express a wide range of
voltage - ***gated*** ***sodium*** ***channel*** alpha-subunits. However, of the auxiliary subunits, beta1 is expressed preferentially in only large- and medium-diameter neurons of the DRG while
beta2 is absent in all DRG cells. In view of this, we have compared the distribution of beta1 in rat DRG and spinal cord with a novel, recently cloned beta1-like subunit, ***beta3*** . In situ hybridization studies demonstrated high levels of ***beta3*** mRNA in small-diameter c-fibres, while beta1 mRNA was virtually absent in these cell types but was expressed in 100% of large-diameter neurons. In the spinal cord, ***beta3*** transcript was present specifically in layers I/II (substantia gelatinosa) and layer X, while beta1 mRNA was expressed in all
laminae throughout the grey matter. Since the pattern of ***beta3*** expression in DRG appears to correlate with the TTX-resistant ***voltage*** - ***gated*** ***sodium*** ***channel*** subunit
PN3, we co-expressed the two subunits in Xenopus oocytes. In this system,
beta3 caused a 5-mV hyperpolarizing shift in the threshold of activation of PN3, and a threefold increase in the peak current amplitude
when compared with PN3 expressed alone. On the basis of these results, we
examined the expression of beta-subunits in the chronic constriction injury model of neuropathic pain. Results revealed a significant increas in ***beta3*** mRNA expression in small-diameter sensory neurons of
the ipsilateral DRG. These results show that ***beta3*** is the dominant auxiliary sodium channel subunit in small-diameter neurons o the
rat DRG and that it is significantly upregulated in a model of neuropathic
pain.

L4 ANSWER 19 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:330120 BIOSIS
DOCUMENT NUMBER: PREV200000330120
TITLE: The voltage-dependent sodium channel subunit ***beta3*** is the predominant beta subunit expressed during development in rat CNS.
AUTHOR(S): Shah, B. S. [Reprint author]; Pinnock, R. D. [Reprint author]; Lee, K. [Reprint author]; Dixon, A. K. [Reprint author]
CORPORATE SOURCE: Parke Davis Neuroscience Research Centre, Cambridge University, Robinson Way, Forvie Site, Cambridge, CB2 2QB, UK
SOURCE: British Journal of Pharmacology, (January, 2000) Vol. 129, No. Proceedings Supplement, pp. 250P. print.
Meeting Info.: Meeting of the British Pharmacological Society. Cambridge, England, UK. January 05-07, 2000. British Pharmacological Society.
CODEN: BJPCBM. ISSN: 0007-1188.
DOCUMENT TYPE: Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Aug 2000
Last Updated on STN: 7 Jan 2002

L4 ANSWER 20 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 12
ACCESSION NUMBER: 2000:399222 BIOSIS
DOCUMENT NUMBER: PREV200000399222
TITLE: The ***voltage*** - ***gated*** ***sodium*** ***channel*** ***beta3*** subunit modulates alphaIII channel gating in Xenopus oocytes.
AUTHOR(S): Stevens, E. B. [Reprint author]; Pinnock, R. D. [Reprint author]; Lee, K. [Reprint author]
CORPORATE SOURCE: Parke Davis Neuroscience Research Centre, Cambridge University, Forvie Site, Cambridge, CB2 2QB, UK
SOURCE: British Journal of Pharmacology, (January, 2000) Vol. 129, No. Proceedings Supplement, pp. 249P. print.
Meeting Info.: Meeting of the British Pharmacological Society. Cambridge, England, UK. January 05-07, 2000. British Pharmacological Society.
CODEN: BJPCBM. ISSN: 0007-1188.
DOCUMENT TYPE: Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Sep 2000
Last Updated on STN: 8 Jan 2002

L4 ANSWER 21 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2000:241776 BIOSIS
DOCUMENT NUMBER: PREV200000241776
TITLE: ***beta3*** , A novel ***voltage*** - ***gated*** ***sodium*** ***channel*** beta subunit, modulates alphaIIA channel gating in Xenopus oocytes.
AUTHOR(S): Morgan, K.; Stevens, E. B. [Reprint author]; Shah, B. S. [Reprint author]; Cox, P. J. [Reprint author]; Dixon, A. K. [Reprint author]; Lee, K. [Reprint author]; Richardson, P. J.; Pinnock, R. D. [Reprint author]; Mizuguchi, K.; Jackson, A. P.
CORPORATE SOURCE: Parke Davis Neuroscience Research Centre, Cambridge University Forvie Site, Robinson Way, Cambridge, CB2 2QB, UK
SOURCE: Journal of Physiology (Cambridge), (Feb., 2000) No. 523P, pp. 160P-161P. print.
Meeting Info.: Joint Meetings of the Physiological Society. Birmingham, England, UK. December 20-22, 1999. The Physiological Society.
CODEN: JPHYA7. ISSN: 0022-3751.
DOCUMENT TYPE: Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Jun 2000
Last Updated on STN: 5 Jan 2002

L4 ANSWER 22 OF 29 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2000:276930 SCISEARCH
THE GENUINE ARTICLE: 294XZ
TITLE: ***beta*** ***3*** , a novel ***voltage*** - ***gated*** ***sodium*** ***channel*** beta subunit, modulates alpha IIA channel gating in Xenopus oocytes
AUTHOR: Morgan K (Reprint); Stevens E B; Shah B S; Cox P J; Dixon A K; Lee K; Richardson P J; Pinnock R D; Mizuguchi K; Jackson A P
CORPORATE SOURCE: UNIV CAMBRIDGE, PARKE DAVIS NEUROSCI RES CTR, CAMBRIDGE CB2 2QB, ENGLAND; UNIV CAMBRIDGE, DEPT BIOCHEM, CAMBRIDGE CB1 1QJ, ENGLAND; UNIV CAMBRIDGE, DEPT PHARMACOL, CAMBRIDGE CB1 1QJ, ENGLAND
COUNTRY OF AUTHOR: ENGLAND
SOURCE: JOURNAL OF PHYSIOLOGY-LONDON, (FEB 2000) Vol. 523, Supp. [S], pp. P160-P161.
Publisher: CAMBRIDGE UNIV PRESS, 40 WEST 20TH STREET, NEW YORK, NY 10011-4211.
ISSN: 0022-3751.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 2

L4 ANSWER 23 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:240738 BIOSIS
DOCUMENT NUMBER: PREV200000240738
TITLE: ***beta3*** Is a novel auxiliary subunit for ***voltage*** - ***gated*** ***sodium*** ***channels*** which exhibits a complimentary distribution to beta1 in adult rat.
AUTHOR(S): Morgan, K.; Stevens, E. B. [Reprint author]; Shah, B. S. [Reprint author]; Cox, P. J. [Reprint author]; Dixon, A. K. [Reprint author]; Lee, K. [Reprint author]; Richardson, P. J.; Pinnock, R. D. [Reprint author]; Mizuguchi, K.; Jackson, A. P.
CORPORATE SOURCE: Parke Davis Neuroscience Research Centre, Cambridge University Forvie Site, Robinson Way, Cambridge, CB2 2QB, UK
SOURCE: Journal of Physiology (Cambridge), (Feb., 2000) No. 523P, pp. 159P-160P. print.
Meeting Info.: Joint Meetings of the Physiological Society. Birmingham, England, UK. December 20-22, 1999. The Physiological Society.
CODEN: JPHYA7. ISSN: 0022-3751.
DOCUMENT TYPE: Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Jun 2000
Last Updated on STN: 5 Jan 2002

L4 ANSWER 24 OF 29 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2000:276929 SCISEARCH
THE GENUINE ARTICLE: 294XZ
TITLE: ***beta*** ***3*** is a novel auxiliary subunit for ***voltage*** - ***gated*** ***sodium*** ***channels*** which exhibits a complimentary distribution to beta 1 in adult rat
AUTHOR: Morgan K (Reprint); Stevens E B; Shah B S; Cox P J; Dixon A K; Lee K; Richardson P J; Pinnock R D; Mizuguchi K; Jackson A P
CORPORATE SOURCE: UNIV CAMBRIDGE, PARKE DAVIS NEUROSCI RES CTR, CAMBRIDGE CB2 2QB, ENGLAND; UNIV CAMBRIDGE, DEPT BIOCHEM, CAMBRIDGE CB1 1QJ, ENGLAND; UNIV CAMBRIDGE, DEPT PHARMACOL, CAMBRIDGE CB1 1QJ, ENGLAND
COUNTRY OF AUTHOR: ENGLAND
SOURCE: JOURNAL OF PHYSIOLOGY-LONDON, (FEB 2000) Vol. 523, Supp. [S], pp. P159-P160.
Publisher: CAMBRIDGE UNIV PRESS, 40 WEST 20TH STREET, NEW YORK, NY 10011-4211.
ISSN: 0022-3751.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 2

L4 ANSWER 25 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:96577 BIOSIS
DOCUMENT NUMBER: PREV200100096577
TITLE: The voltage-gated Na+ channel ***beta3*** subunit is present in human skeletal muscle and functionally couples with the alpha subunit, SkM1.
AUTHOR(S): Shah, B. S. [Reprint author]; Cox, P. J. [Reprint author]; Stevens, E. B. [Reprint author]; Dixon, A. K. [Reprint author]; Richardson, P. J.; Pinnock, R. D. [Reprint author]; Lee, K. [Reprint author]
CORPORATE SOURCE: Parke-Davis Neuroscience Research Centre, Cambridge University Forvie Site, Robinson Way, Cambridge, CB2 2QB, UK
SOURCE: Journal of Physiology (Cambridge), (2000) Vol. 528P, pp. 88P. print.
Meeting Info.: Scientific Meeting of the Physiological Society. Aberdeen, Scotland, UK. September 06-08, 2000. The Physiological Society.
CODEN: JPHYA7. ISSN: 0022-3751.
DOCUMENT TYPE: Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Feb 2001
Last Updated on STN: 15 Feb 2002

L4 ANSWER 26 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 13
ACCESSION NUMBER: 2000:353988 BIOSIS
DOCUMENT NUMBER: PREV200000353988
TITLE: ***Beta3*** , a novel auxiliary subunit for the ***voltage*** ***gated*** ***sodium*** ***channel*** is upregulated in sensory neurones in the chronic constriction injury model of neuropathic pain.
AUTHOR(S): Shah, B. S. [Reprint author]; Gonzalez, M. I. [Reprint author]; Bramwell, S. [Reprint author]; Pinnock, R. D. [Reprint author]; Lee, K. [Reprint author]; Dixon, A. K. [Reprint author]
CORPORATE SOURCE: Parke Davis Neuroscience Research Centre, Robinson Way, Cambridge, UK
SOURCE: European Journal of Neuroscience, (2000) Vol. 12, No. Supplement 11, pp. 70. print.
Meeting Info.: Meeting of the Federation of European Neuroscience Societies. Brighton, UK. June 24-28, 2000.
ISSN: 0953-816X.
DOCUMENT TYPE: Conference; (Meeting) Conference; Abstract; (Meeting Abstract) Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Aug 2000
Last Updated on STN: 8 Jan 2002

L4 ANSWER 27 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:114998 BIOSIS
DOCUMENT NUMBER: PREV200100114998
TITLE: Modulation of Na+ channels by beta1, beta2 and ***beta3*** subunits in tsA-201 cells.
AUTHOR(S): Qu, Y. [Reprint author]; Westenbroek, R.; Scheuer, T.; Curtis, R.; Catterall, W. A.
CORPORATE SOURCE: U. of Washington, Seattle, WA, USA
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-713.4. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 04-09, 2000.
Society for Neuroscience.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Mar 2001
Last Updated on STN: 15 Feb 2002
AB Voltage-gated neuronal Na+ channels consist of a pore-forming alpha subunit associated with auxiliary beta subunits (e.g., beta1, beta2, and ***beta3*** subunits) that alter channel function. ***beta3*** is a newly discovered beta subunit most closely related to beta1. To examine the functional consequences of beta subunit coexpression, we cotransfected tsA-201 cells with rat brain type IIA Na+ channel alpha subunits alone, with one of the beta subunits, or with the combinations beta1 + beta2 or beta2 + ***beta3*** . Transfection of each beta subunit or beta pair with the alpha subunit caused depolarizing shifts in the voltage dependence of both activation and inactivation. The ***beta3*** or beta2 + ***beta3*** caused the largest shifts (apprx+12 mV). Cotransfection of beta1, beta2 or beta1 + beta2 with alpha did not change the rate of current inactivation during pulses to positive potentials and there was little non-inactivating current. In contrast, cotransfection of ***beta3*** or beta2 + ***beta3*** with alpha caused slowed inactivation of current during depolarizations and inactivation was less complete (4.5% vs 1.2 sustained current). The effects of beta subunits on voltage-dependence in tsA-201 cells differed from their effects in Xenopus oocytes or Chinese Hamster ovary cells where beta subunit expression causes negative shifts in voltage dependent parameters. Thus, cellular environment is critical for determining channel properties and their modulation by beta subunits. The ***beta3*** subunit has the additional and novel effect of favoring sustained, non-inactivating Na+ current. Such sustained Na+ current is proposed to play important neurophysiological roles. Our data identify the specific complement of beta subunits as being a key factor affecting Na+ channel phenotype.

L4 ANSWER 28 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:107940 BIOSIS
DOCUMENT NUMBER: PREV200100107940
TITLE: Cloning and localization of a novel Na+ channel ***beta3*** subunit.
AUTHOR(S): Curtis, R. A. [Reprint author]; Lawson, D.; Ge, P.; DiStefano, P. S.; Silos-Santiago, I.
CORPORATE SOURCE: Millennium Pharmaceuticals, Cambridge, MA, USA
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-418.22. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 04-09, 2000.
Society for Neuroscience.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Feb 2001
Last Updated on STN: 15 Feb 2002
AB We have cloned a novel auxiliary ***beta3*** subunit of ***voltage*** - ***gated*** ***sodium*** ***channels*** from a rat dorsal root ganglion library. The predicted protein is structurally related to the previously cloned beta1 and beta2 subunits and also shares 50% sequence homology with the beta1 subunit. In situ hybridization analysis in sections of human, monkey and rat brain shows that this gene is highly expressed in CA layers of hippocampus, in the subiculum and in cerebellar Purkinje cells. In the cortex, expression is heaviest in layers I-II with lower levels in layers IV-VI. Low levels of expression are found in the striatum. In the spinal cord, the ***beta3*** subunit is mainly expressed in grey matter regions thought to be involved in nociceptive processing (laminae I-II, V and around the central canal) but not in motor neurons. In the peripheral nervous system, ***beta3*** subunit is also detected in neuronal populations involved in nociception There is widespread expression of ***beta3*** subunit in sympathetic neurons of the superior cervical ganglion. In sensory neurons of the dorsal root ganglion, expression is restricted to neurons of both small and medium size, whereas large proprioceptive neurons do not express the ***beta3*** subunit. These results, as well as electrophysiological evidence (Y. Qu, R. Westenbroek, T. Scheuer, R. Curtis and W.A. Catterall, presented at this meeting), suggest that ***beta3*** subunit may modulate sodium currents in neurons involved in nociceptive pathways. We are currently investigating the regulation of this gene in different models of inflammatory and neuropathic pain.

L4 ANSWER 29 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:88476 BIOSIS
DOCUMENT NUMBER: PREV200100088476
TITLE: ***beta3*** , An auxiliary subunit of the ***voltage*** ***gated*** ***sodium*** ***channel*** is upregulated in sensory neurones in two models of neuropathic pain.
AUTHOR(S): Shah, B.; Gonzalez, M. I.; Bramwell, S.; Rock, D.; Pinnock, R. D.; Lee, K.; Dixon, A. K.
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-352.6. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 04-09, 2000.
Society for Neuroscience.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Feb 2001
Last Updated on STN: 12 Feb 2002
AB Rat brain ***voltage*** ***gated*** ***sodium*** ***channels*** are composed of a pore-forming alpha subunit and two auxiliary subunits, beta1 and beta2. Recently we have identified a novel beta subunit, ***beta3*** , which is related to beta1 exhibiting 50% homology. We have examined the distribution of beta1 and

beta3
in rat DRG and spinal cord by in situ hybridisation following the chronic constriction injury (CCI) and streptozocin (STZ) (diabetic neuropathy) models of neuropathic pain. CCI was performed on the ipsilateral sciatic nerve. Diabetes was induced in rats by an i.p. injection of streptozocin (50mg/kg). In situ hybridisation was carried out on dorsal root ganglion (DRG) and spinal cord slices and quantification performed on an MCID image analyser. Following CCI surgery, beta1 mRNA expression showed no change in DRG or spinal cord. In contrast ***beta3*** mRNA significantly increased ($p<0.005$) in ipsilateral small sensory c-fibres of the DRG compared to the contralateral side. Following STZ treatment, beta1 message appeared unchanged in any cell types examined whilst ***beta3*** mRNA expression increased significantly ($p<0.05$) in medium diameter Adelta fibres in treated DRGs in comparison to sham controls. ***beta3*** mRNA also significantly increased ($p<0.05$) in layers I/II (substantia gelatinosa)of the spinal cord of STZ treated animals compared to shams.

In conclusion, ***beta3*** message is differentially upregulated in sensory neurones in the CCI and STZ models of neuropathic pain highlighting the different mechanisms that may occur in these models.